Clinicopathologic Session

Case 6/99 - The patient is a 46-year-old female with marked myocardial hypertrophy and heart failure - Heart Institute (InCor) - Fac. Med USP (Br)

A 46-year-old female patient sought medical assistance because of dyspnea on minimum exertion.

The patient first had dyspnea and edema during pregnancy at the age of 29 years, when heart disease was diagnosed. After the delivery, she remained asymptomatic and underwent cardiological assessment. An echocardiogram at that time (July '80) showed asymmetrical myocardial hypertrophy and alteration in the mobility of the anterior cusp of the mitral valve, suggesting a disorder in ventricular compliance. The measures are shown in table I. The patient was regularly followed up with clinical and echocardiographic evaluations (table I).

After 2 years, the patient underwent cardiac catheterization (January '82), which revealed normal coronary arteries and right and left ventricular hypertrophy. Simultaneous biventricular injection did not show disproportion between the thickness of the interventricular septum and that of the posterolateral wall of the left ventricle (table II).

The patient's brother had hypertrophic cardiomyopathy and underwent heart transplantation due to heart failure. The patient was informed that her heart disease was familial and she remained asymptomatic.

One year ago she was diagnosed with diabetes mellitus, and dyspnea triggered by exertion appeared and progressively increased.

On electrocardiogram (August '96), she had sinus rhythm, a heart rate of 103 bpm, supraventricular extrasystoles, SAP +90° forward, QRS axis -60° forward, right atrium overload, left anterosuperior division bundle-branch block, anterior position of the QRS loop, presence of deep Q-waves in the V5, V6, I and aVL leads, and decrease in the left ventricle potentials in these same leads (fig. 1).

On echocardiogram (August '96), she had concentric myocardial hypertrophy with no signs of obstruction of the left ventricle outflow tract. In spite of the preserved dimensions of the left ventricle (table I), akinesia of a small portion of the inferior wall of the left ventricle and marked hypokinesia of the posterolateral wall of the left ventricle existed.

A new electrocardiogram (May '97) showed sinus rhythm, a heart rate of 100 bpm, QRS axis forward and undetermined in the frontal plane, biatrial overload, and a pattern considered suggestive of asymmetric septal hypertrophy.

A recent medical evaluation included an echocardiogram (July '97) showing a left ventricle shortening fraction of 28%, a relation of 3.6 between the thicknesses of the interventricular septum and the posterior wall of the left ventricle, and a pulmonary artery systolic pressure of 58 mmHg estimated by Doppler. Moderate concentric hypertrophy of both ventricles occurred, as did akinesia of the inferior wall of the left ventricle and hypokinesia of the lateral wall of the left ventricle. No signs of obstruction of the left ventricle outflow tract existed. Signs of mild mitral and tricuspid regurgitation were observed.

In August '97, dyspnea began to be triggered by minimum exertion, being accompanied by palpitations and edema of the lower limbs.

A chest x-ray (August '97) revealed mild enlargement of the cardiac area.

Laboratory findings (August '97) were as follows: hemoglobin, 18.5 g/dL; hematocrit, 60%; creatinine serum levels, 1.4 mg/dL; sodium, 138 mEq/L; potassium, 4.3 mEq/L; and glycemia, 133 mg/dL.

The patient was taking daily 40 mg of furosemide, 100 mg of spironolactone, 0.25 mg of digoxin, 20 mg of enalapril, 200 mg of amiodarone, and 15 units of slow-release human insulin. Despite the medicamentous treatment, the patient's clinical condition got worse and she was referred to the (Heart Institute (InCor)).

On physical examination (September '97), the patient showed a regular condition, tachypnea (26 respiratory incursions per minute), a regular pulse of 90 bpm, blood pressure of 120/80 mmHg. Venous jugular pressure was elevated ++/4+. The lungs were normal and the heart did not reveal any abnormality. The liver could be palpated 3 cm from the right costal margin and edema of the lower limbs (++/4+) occurred, with no signs of deep venous thrombosis.

The patient was admitted to the hospital to control heart failure attributed to hypertrophic cardiomyopathy. The following medications were prescribed: enalapril, 5 mg; propranolol, 80 mg; furosemide, 80 mg by oral via; and insulin, 15 units by subcutaneous via every day.

Fifteen hours after admission, the patient developed severe dyspnea and profuse sweating, signs of peripheral hypoperfusion, and arterial hypotension. The heart rate monitored by electrocardiography was 20 bpm. The patient, then, had a cardiac arrest in asystole refractory to resuscitation maneuvers and died.

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Table I - Echocardiograms

Chamber	July '80	July '81	June '93	August '96
Aorta (mm)	16	32	36	32
Left atrium (mm)	30	32	39	39
Left ventricle				
Diastolic diameter (mm)	34	35	40	36
Systolic diameter (mm)	21	25	26	
Ejection fraction	0.76	0.67	0.75	0.62
Septum thickness (mm)	23	18	24	15
Posterior wall (mm)	16	11	13	14
Anterior movement of the mitral valve	No	No	No	No
Right ventricle (mm)	18	18	19	17
Pulmonary systolic pressure (mmHg)	-	-	Normal	49

Table II – Data of the cardiac catheterization (pressures in mmHg)

Pressures	Systolic	Initial diastolic	Final diastolic	Mean
Right atrium				11
Right ventricle	50	12	20	
Pulmonary artery	50	28		38
Pulmonary occlusion				23
Left ventricle	122	21	38	
Aorta	122	76		96

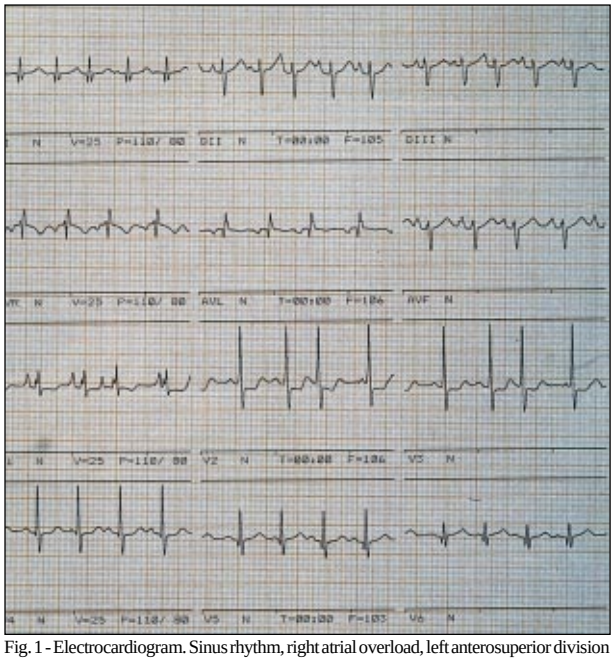

Fig. 1 - Electrocardiogram. Sinus rhythm, right atrial overload, left anterosuperior division bundle-branch block, anterior position of the QRS loop, and inactive lateral area.

Discussion

Clinical aspects – the patient is a 46-year-old female diagnosed with hypertrophic cardiomyopathy in its familial and nonobstructive form.

The initial symptoms (edema and dyspnea) appeared at the age of 29 years during pregnancy. There is no report in the literature on pregnancy precipitating the initial symptoms of hypertrophic cardiomyopathy. It seems clear, however, that the physiological hemodynamic alterations that occur during pregnancy, such as increase in blood volume, in venous return, and in the cardiac output, and decrease in the peripheral vascular resistance, especially from the second trimester on, can induce symptom onset (dyspnea, edema) in patients with hypertrophic cardiomyopathy.

After delivery, the patient became asymptomatic and remained so for 16 years, then with the diagnosis of hypertrophic cardiomyopathy but with no medication. One year ago, she started to develop dyspnea on exertion, which progressed to dyspnea on minimum exertion and at rest, accompanied by palpitations and edema of the lower limbs.

In regard to the causes of the onset and rapid progression of symptoms in the last 12 months, we can formulate many diagnostic hypotheses.

The symptoms could result from diastolic dysfunction, which is the main characteristic of this disease, leading to an increase in ventricular filling pressures or progression of the disease to the dilated form. This form of the disease occurs in 10% to 15% of patients, with enlargement of the left ventricular cavity, thinning of the ventricular walls, reduction in the ejection fraction, or a combination of these abnormalities, such as the disappearance of the gradient of the left ventricular outflow tract [1].

The patient's brother underwent cardiac transplantation because of heart failure, and this may have resulted from progression of the disease to its dilated form. The familial form of hypertrophic cardiomyopathy with dominant autosomal genetic transmission accounts for 50% of patients with this disease.

In a study [1] of 128 patients from 7 families with the genetic form of the hypertrophic cardiomyopathy defined by sudden death or progression to the final phase of dilation in relatives of the patients, 26 sudden deaths and 9 progressions to the final phase of dilation were observed. The patients with sudden death were younger (23±11 years) than those patients who needed cardiac transplantation or died in the final phase (42±8 years). The study showed that members of the same family with hypertrophic cardiomyopathy, despite their common genetic substrate, may show distinct expressions of the natural history of the disease, which occur in different periods of life.

Our patient died at the age of 46 years in cardiac failure, and she might have had the longer-lasting form of the disease, even though no ventricular dilation had been detected.

Another cause might be the association of obstructive coronary artery disease because the electrocardiogram revealed deep Q-waves in V5, V6, I, and aVL, and decrease in the left ventricle potentials in these leads. These alterations may have resulted only from left ventricular hypertrophy of the hypertrophic cardiomyopathy or from acute myocardial infarction of the inferolaterodorsal wall, which is still suggested by the echocardiographic findings of akinesia of the inferior wall of the left ventricle and marked hypokinesia of the posterolateral wall of the left ventricle.

One study [1] showed that the association of coronary artery disease with hypertrophic cardiomyopathy may be lethal. In 16 patients, 5 (30%) sudden deaths were observed in patients above 40 years of age, all of whom had critical coronary obstructions.

In regard to the cause of death, our patient died because of heart failure, which is observed in 10% to 15% of the patients, because sudden death is the most common form of death in these patients [1,2].

Association of arrhythmias with hypertrophic cardiomyopathy is frequent; ventricular arrhythmias are present in more than 75% of the patients, nonsustained supraventricular tachycardia in 30%, and atrial fibrillation in 10% of the patients [3,4].

In regard to sudden death, several studies have shown the relation between sudden death and ventricular arrhythmias. The presence of ventricular tachycardia on long-term electrocardiogram, even in the absence of symptoms, has been associated with an increase in the incidence of sudden death in patients with hypertrophic cardiomyopathy [3,4]. Sudden death was 8 times more frequent (24% vs 3%) when ventricular tachycardia occurred [4]. However, the fact that sudden death did not occur in 13 out of the 17 patients with ventricular tachycardia suggests that other variables may coexist in patients with hypertrophic cardiomyopathy, so that ventricular instability evolves to a terminal arrhythmia [4].

With the use of beta-blockers, supraventricular arrhythmias significantly decrease, but a reduction in the frequency of ventricular arrhythmias does not occur [3]. A case of sudden death due to ventricular tachycardia has been reported, which degenerated to ventricular fibrillation on long-term electrocardiogram in a patient after beginning to use atenolol [5].

Our patient had palpitations on exertion and used amiodarone but did not undergo monitoring with long-term electrocardiogram. So far, the evidence of the role of amiodarone in preventing sudden death in patients with hypertrophic cardiomyopathy remains controversial [6-8], in spite of its proved efficacy in the treatment of complex ventricular arrhythmias in the ADEG study [9].

Arrhythmia is the most common cause of sudden death in patients with hypertrophic cardiomyopathy and may be due to the proarrhythmic effects of the drugs used in the treatment. They include monomorphic or polymorphic sustained ventricular tachycardia, ventricular fibrillation, atrial tachycardia, atrial flutter, asystole, bradyarrhythmias, and diseases of the conducting system.

Patients with hypertrophic cardiomyopathy are very sensitive to oscillations in heart rate and to the loss of atrial contribution to ventricular filling. Therefore, all these arrhythmias are potentially lethal and may lead to arterial hypotension, myocardial ischemia, hemodynamic instability, and sudden death.

In conclusion, the diagnostic hypotheses for the triggering factor of sudden death in our patient are as follows: 1) arrhythmias, based on what was previously revealed; 2) complicated acute myocardial infarction, such as acute mitral regurgitation (due to dysfunction or rupture of the papillary muscle), rupture of the free wall, or arrhythmia; 3) acute pulmonary thromboembolism; 4) spontaneous hypertensive pneumothorax.

(Dr. Mauro Sergio Stateri Carvalho)

Autopsy

The heart weighed 500 g. The left ventricle exhibited marked symmetric hypertrophy of the walls without dilation of the cavity. The right cardiac chambers were hypertrophied and mildly dilated (fig. 2). Examination of the aorta revealed coarctation of the aortic arch located at the isthmic region with marked stenosis of the aortic lumen. Pre- and poststenotic dilation and atherosclerotic plaques at the isthmic region were seen; the ductus arteriosus was closed and composed of the arterial ligament (figs. 3 and 4). The aortic valve was bicuspid, but showed a good coaptation of the semilunar leaflets, without fibrous thickening or calcification. The other cardiac valves and coronary arteries did not show any abnormality. On histological examination, the cardiomyocytes were hypertrophied, and small and sparse areas of focal ventricular myocardial fibrosis (cardiomyosclerosis) could be seen.

The lungs and liver showed alterations secondary to

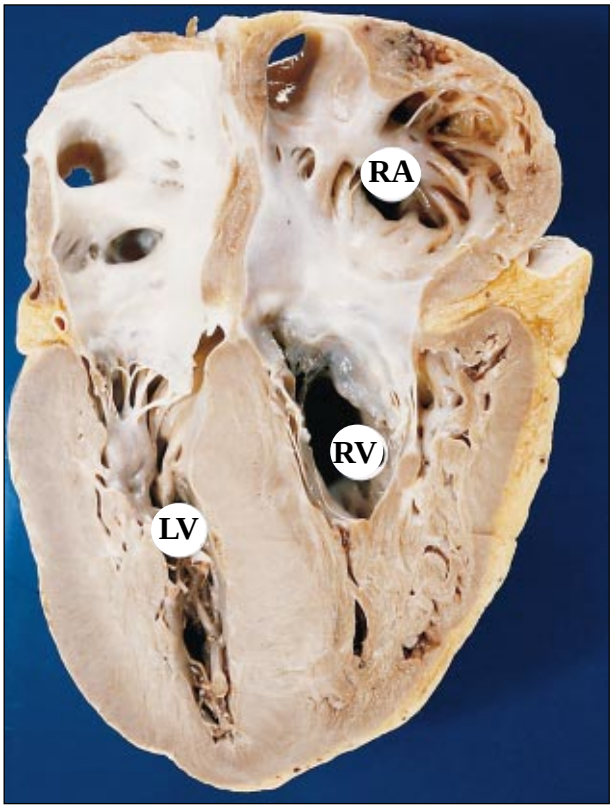

Fig. 2 - Longitudinal section of the heart, showing the 4 chambers. Marked concentric and symmetric hypertrophy of the left ventricle (LV) can be seen. Right atrium (RA) and ventricle (RV) show hypertrophy and mild dilation.

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Fig. 3 – View of the internal aspect of the aortic arch and beginning of the descending thoracic aorta. Observe the stenotic aortic lumen in the region of coarctation (asterisk) and the fold in the aortic arch wall, comprising the coarctation (arrow heads). Pre- (star) and poststenotic (double star) dilations are evident.

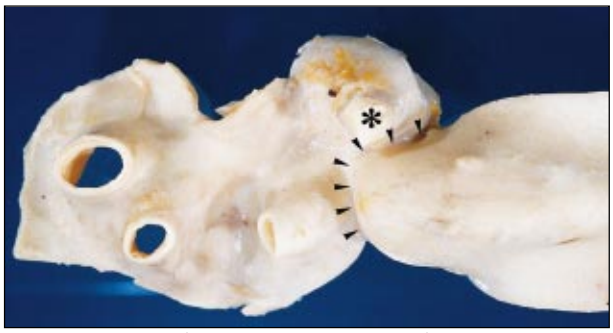

Fig. 4 – External view of the aortic arch and beginning of the descending thoracic aorta. Note the groove corresponding to the region of coarctation (arrow heads) and the arterial ligament (asterisk).

chronic passive congestion. A bilateral pleural effusion composed of clear yellow liquid (1,200 mL) was detected and also cerebral edema.

(Dr. Luiz Alberto Benvenuti)

Diagnoses - Coarctation of the aortic arch, concentric left ventricular hypertrophy, bicuspid aortic valve.

Comments

This is a case of marked concentric and symmetric hypertrophy of the left ventricle due to coarctation of the aortic arch, whose clinical diagnosis was hypertrophic cardiomyopathy. This clinical diagnosis could not be morphologically confirmed because the myocardial hypertrophy observed in hypertrophic cardiomyopathy is, by definition, primary, and it cannot be attributed to ventricular overload resulting from pressure or volume[10].

Coarctation of the aortic arch, particularly when associated with marked stenosis of the aortic lumen, as in the present case, obviously causes left ventricular overload. The marked ventricular hypertrophy resulted in heart failure, probably diastolic due to absence of ventricular dilation, with consequent chronic passive congestion of the lungs and liver. Ventricular arrhythmia, which might have been the terminal cause of the patient's death, may be related to intense myocardial hypertrophy and the presence of small foci of ventricular fibrosis (cardiomyosclerosis).

A congenital alteration frequently associated with coarctation of the aortic arch with a closed ductus arteriosus, present in this case, is the bicuspid aortic valve [11]. We should stress, however, that in this case no morphological evidence of dysfunction of this valve existed.

(Dr Luiz Alberto Benvenuti)

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